Master 2 PROJECT

Characterization of a novel pathway regulating the skeletal muscle mass using proteomic approaches

Muscle wasting occurs in many diseases and systematically in older people. It corresponds to the loss of muscle mass that reduces the quality of life and contributes to mortality. In order to fight this major public health concern, it is necessary to identify and to understand its mechanisms of control. One of them is the ubiquitin-mediated degradation of proteins by the proteasome (Hnia et al., 2019). We have identified the Asb2ß protein (Bello et al., 2009), which is an actor of this system and a novel regulator of muscle mass (Davey et al., 2016). Its overexpression is sufficient to induce muscle atrophy in mice (Davey et al., 2016). Our ongoing project is to decipher Asb2ß's mechanisms of action through the identification of its targets, which are polyubiquitylated and degraded by the proteasome. To reach this aim, we have generated a mouse model that allows the conditional invalidation of ASB2 gene in adult skeletal muscles. By comparing the proteome and the the ubiquitinome of muscles expressing or not Asb2ß, we will identify putative Asb2ß's targets. The specific aim of the Master project is to perform quantitative proteomic analysis using label free or tag (TMT) tandem mass spectrometry (Tandem Mass Tag) of skeletal mouse muscles expressing or not Asb2ß. The next step will be to validate these substrates using biochemical and cell biology approaches. This project should unravel potential therapeutic target to fight muscle wasting.

Techniques used during the internship:

- Biochemical methods for analysis and purification of proteins and peptides (electrophoresis, western-blot, immunopurification …)
- Bottom-up mass spectrometry analysis (nanoHPLC ESI-MS/MS on different types of Orbitrap mass spectrometers),
- Mass spectrometry-based differential quantification and statistical analysis,
- Bioinformatic analysis for data treatment and data mining.

Bibliography:

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